Perchlorate and Human Health: Literature Summary

Perchlorate and the Human Adult:

The thyroid gland makes thyroid hormone that circulates in the blood and regulates tissue metabolism, particularly protein synthesis. The thyroid gland concentrates iodine from the blood, iodinates tyrosine, and subsequently generates the thyroid hormones (T_4 and T_3) within the large glycoprotein thyroglobulin. T_4 and T_3 are then hydrolyzed and secreted into the blood. A large store of preformed hormone is present in the thyroid.

Anti-thyroid drugs act by either blocking the uptake of iodine or by blocking the synthesis of T_4 and T_3. Perchlorate's effect on the thyroid has been well studied (Wolff, 1998). It is a competetive inhibitor for iodine uptake by the thyroid and does not affect the synthesis of thyroid hormone. Perchlorate is the most effective drug at blocking the uptake of iodine. It is a competitive inhibitor for iodine uptake. Perchlorate passes rapidly through the body. The half-life ($T_{1/2}$) for perchlorate in humans is about 6 hours (Eichler, 1929). Ninety-five percent of the ingested dose is excreted as perchlorate into the urine. The thionamides (such as carbimazole, MMI [Tapazol], or PTU) are effective at blocking hormone synthesis. In some cases of thyrotoxicosis, both types of drugs are given simultaneously.

Perchlorate was used for treating thyrotoxicosis (hypothyroidism) in the 1950s. After a few cases of fatal aplastic anemia or agranulocytosis in patients treated with very large doses of perchlorate (600-1600 mg/day) for long durations (months) in the early to mid 1960s, its use diminished. No case of fatal aplastic anemia or fatal agranulocytosis has been reported in a patient receiving less than 600 mg/day perchlorate (Rokke and Vogt, 1968). There is a case report of a lady who was successfully treated with 200 mg/day perchlorate for 22 years without complications (Connell, 1981).

Currently, perchlorate is used for patients who are sensitive to the other drugs and, particularly, for patients who suffer from iodine-induced thyrotoxicosis. Doses of 800 mg/day perchlorate are recommended for patients with sensitivity to other drugs (Evered, 1976). The drug amiodarone is used to treat heart patients with ischemic heart disease or, more commonly, those with rapid heart beats (tachycardia). Amiodarone may be a life-saving drug; however, because it contains nearly 40 percent iodine, it can be toxic to the thyroid gland. Case series of patients with amiodarone associated thyrotoxicosis (AAT) have been published for patients treated for nearly a month or more with 1,000 mg/day perchlorate and had no adverse effect on their blood cells (Martino et al, 1986a, 1986b; Richert et al, 1989; Trip et al., 1994). There is a report of one patient who developed a mild neutropenia after forty days of treatment at 1,000 mg/day perchlorate (Martino et al., 1986b).

A small block in iodine uptake (such as by perchlorate) is likely to be compensated by the thyroid. For example, a study in Austria showed that nearly 40 percent of euthyroid people had normal thyroid levels in spite of having low iodine intake (< 100 ug/l/gm creatinine in the urine) (Buchinger et al., 1997). Similarly, a study in Sweden showed that milk-containing thiocyanate (8 mg per day for 12 weeks) did not affect the thyroid hormone

status (blood T_3, T_4, and TSH) in women (Dahlberg et al, 1994). Thiocyanate is both an antithyroid drug and a bacteriostatic agent. The thyroid regulation system is usually able to maintain a normal thyroid hormone level unless the thyroid is completely blocked from the uptake of iodine for a prolonged period of time.

Perchlorate and the Human Fetus:

Historically, perchlorate has specifically been used for the treatment of thyrotoxicosis in pregnancy. Thus, the evidence of the effect of perchlorate on the human fetus comes from these patients. Crooks and Wayne (1960) reported in Lancet that

> "Opinion is almost unanimous that the most appropriate form of therapy for women who develop thyrotoxicosis during pregnancy is the administration of an antithyroid drug. Goitre and hypothyroidism have been reported in the infants of mothers who have received these substances but it is rare, and when it occurs the dosage has almost always been unduly high (Macgregor and Goodwin, 1953). We have treated 12 pregnant thyrotoxic patients with potassium perchlorate (600 mg/day or 1000 mg/day) and in each have achieved satisfactory control of the disease. One of the infants had a very slight enlargement of the thyroid which disappeared within 6 weeks. The remainder showed no abnormality of any kind. We report these results to show that the different mode of action of potassium perchlorate and its special physical properties do not render it more liable to affect the foetal thyroid than the antithyroid substances in more common use."

The concern about perchlorate and the fetus is that it might present the possibility of congenital hypothyroidism with mental retardation (cretinism). This is a severe form of mental retardation that is found in areas with endemic iodine deficiency. In these cases, the fetus has exceptionally low iodine exposure both in utero and after birth. That is not the situation anywhere in the United States. The United States diet is not iodine-deficient, and all states have neonatal screening programs that detect early cases of congenital hypothyroidism.

Congenital hypothyroidism is found in approximately 1 in 3500 live births, but is easily detected and readily treated among children born in hospitals throughout the United States. In counties in California that reported cases of congenital hypothyroidism in 1996, the rates were no higher in counties reporting perchlorate in drinking water or wells as compared to counties that did not (Lamm, 1998).

Newborn infants with congenital hypothyroidism who are identified by screening programs and treated promptly usually have IQs in the normal range at five to seven years of age, as well as normal growth and development. Even children born without a thyroid have normal intellect if thyroid treatment starts early (Burrows et al, 1994). The thyroid system of the fetus develops independently of the mother's, although it is dependent on the maternal-placental system for adequate iodine supply (Fisher DA, 1997). Even in the absence of a functioning fetal thyroid, the maternal thyroxine that crosses the placenta is usually able to sustain a fetal blood level of 40-60 nmol/liter (Vulsma et al., 1989; Larsen

PR, 1989). The maternal thyroxine is generally sufficient to supply enough thyroid hormone to the fetus to take care of the fetal brain, although the fetal thyroid hormone levels are lower than normal. Children's IQs are generally normal if the newborn's thyroxine level is 43 nmol/liter or higher (Tillotson et al., 1994) and if the post-natal treatment is sufficient to restore the serum TSH to normal levels (about 6-11 ug L-thyroxine/kg/day; Illicki and Larsson, 1991). Fetuses with a normal fetal thyroid whose mothers are taking anti-thyroid medications have normal levels of thyroid hormones (Momotani et al, 1997). Studies of children born to mothers who were treated with anti-thyroid drugs during pregnancy have normal IQs (not different from comparison children) (Burrow et al., 1978; McCarroll et al., 1976; and Messer et al., 1990).

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